Research / Recherche

Risk of vaccine-associated paralytic poliomyelitis in Latin America, 1989–91

J.K. Andrus,[1] P.M. Strebel,[2] C.A. de Quadros[3] & J.-M. Olivé[4]

A major factor influencing the success of poliomyelitis eradication in the Americas was the reliance on mass immunization campaigns with oral poliovirus vaccine (OPV). As global poliomyelitis eradication activities accelerate and campaign vaccine delivery strategies are applied elsewhere, it is critical to determine whether the risk of vaccine-associated paralytic poliomyelitis (VAPP) is altered when routine delivery strategies are supplemented with mass immunization campaigns. We analysed all 6043 cases of acute flaccid paralysis (AFP) reported in Latin America over the period 1989–91 in order to estimate the risk of VAPP. The overall risk was estimated to be one case per 1.5–2.2 million doses of OPV administered, compared with one case per 1.4 million doses administered in England and Wales (1985–91) and with one case per 2.5 million net doses distributed in the USA (1980–89). These data suggest that to eradicate poliomyelitis globally, strategies that rely on mass immunization campaigns to supplement routine delivery services, as recommended by WHO, do not appear to alter significantly the risk of VAPP.

Introduction

The last case of culture-confirmed poliomyelitis in the Region of the Americas was reported in Peru on 23 August 1991, suggesting that transmission of indigenous wild poliovirus is on the verge of being eradicated from the hemisphere (*1*). This success comes a mere 6 years after the initiative to eradicate poliomyelitis was adopted by the Pan American Health Organization (PAHO) in 1985 (*2*). Eradication was essentially accomplished by the following approach: aggressive surveillance for cases of acute flaccid paralysis (AFP); supplementation of routine immunization with mass immunization campaigns, such as house-to-house delivery of oral poliovirus

[1] Medical Epidemiologist, Expanded Programme on Immunization, WHO Regional Office for South-East Asia, Indraprastha Estate, Mahatma Gandhi Road, New Delhi 110002, India. Requests for reprints should be sent to this address.

[2] Medical Epidemiologist, National Immunization Program, Centers for Disease Control and Prevention, Atlanta, GA, USA.

[3] Senior Regional Advisor, Pan American Health Organization, Washington, DC, USA.

[4] Regional Advisor, Pan American Health Organization, Washington, DC, USA.

vaccine (OPV) in high-risk areas and national immunization days held twice yearly in most countries; and achievement and maintenance of high OPV coverage (*3, 4*).

For the past 30 years, the USA has also relied primarily on use of OPV to control poliomyelitis. However, one disadvantage associated with OPV is the rare occurrence of vaccine-associated paralytic poliomyelitis (VAPP). The overall risk of VAPP has been estimated to range from one case per 2.5 million net doses distributed in the USA (1980–89), to one case per 1.4 million doses administered in England and Wales (1985–91); in these countries OPV is currently delivered solely through the routine health services (*5, 6*). Since only single-dose vials of OPV are used in the USA, and unused doses of vaccine are returned to the manufacturer and a reimbursement paid (private sector only), the number of doses of OPV administered is very close to the net doses distributed.

As other regions of the world embark upon poliomyelitis eradication using the successful strategies developed by PAHO, it is important to determine whether the risk of VAPP is altered when routine delivery strategies are supplemented with mass immunization campaigns. To that end, we estimated the risk of VAPP in Latin America, employing data collected

by the AFP surveillance system used to monitor the eradication of poliomyelitis in Latin America (4).

Methods

Case finding and case investigation

Suspected poliomyelitis cases are reported and investigated when acute onset of paralysis occurs in a person less than 15 years of age for any reason other than severe trauma, or when a person of any age develops a paralytic illness that is suspected to be poliomyelitis.

Probable poliomyelitis, or AFP, is defined as any suspected case in which the paralysis is flaccid and for which no cause other than poliomyelitis can clearly be identified. AFP is a reportable condition in all countries of Latin America.

For purposes of this analysis, compatible poliomyelitis was defined as any person with AFP who had residual paralysis clinically compatible with poliomyelitis 60 days after paralysis. Confirmed poliomyelitis was any case of AFP with wild-type poliovirus isolated from the stool specimens taken from the patient or the patient's contacts.

All cases of AFP reported to the ministries of health in Latin American countries from January 1989 to December 1991 were included in the analysis. Information available on these patients included demographic data, clinical symptoms and signs, laboratory results, and the final clinical diagnosis.

Recipient VAPP is currently defined by PAHO as any case of AFP with onset of paralysis at an interval of 4–30 days following receipt of OPV and the presence of neurological sequelae compatible with poliomyelitis 60 days following paralysis onset and isolation of vaccine-related poliovirus from the stools. In the USA, the interval used to define cases of recipient VAPP has traditionally been 4–30 days prior to onset of "symptoms", rather than onset of "paralysis". Early symptoms, such as headache or sore throat, may precede paralysis by 1–10 days (7, 8). Hence, for the present analysis the interval used to define a recipient case was 4–40 days between receipt of OPV and onset of paralysis. The results are then comparable to those of other studies. Alternative intervals, including 4–30 and 4–45 days, were also examined. In our analysis, recipient VAPP was not dependent upon isolation of vaccine-related poliovirus or age.

Limited information is available in the PAHO database to define contact VAPP cases by history of exposure to another child who received OPV. However, the database contains all cases of AFP reported in the Americas from 1989 to 1991, and contact

VAPP is a subset of this. Contact VAPP was therefore defined as any case of AFP with neurological sequelae 60 days after paralysis onset (excluding recipient VAPP and culture-confirmed cases of poliomyelitis), and from whose stools vaccine-related poliovirus was isolated.

Some of the recipient and contact VAPP cases had other diagnoses such as Guillain-Barré syndrome (GBS), transverse myelitis, tumour, or trauma, which are unlikely to be etiologically related to OPV. Because the presence of fever at paralysis onset with neurological sequelae 60 days after paralysis onset is a risk factor for culture-confirmed poliomyelitis in the Americas (9), the presence of fever at paralysis onset was compared for patients diagnosed to be clinically compatible with poliomyelitis versus those diagnosed to have GBS.

Isolation of poliovirus from stool specimens

Viruses were isolated from stool suspensions by culture in a rhabdomyosarcoma and Hep-2C cell monolayer, using standard procedures (10).[a] After their serotype had been determined by neutralization tests using high-titre equine sera, poliovirus isolates were further characterized as vaccine-related or wild by hybridization with genotypic probes (11 and by polymerase chain reaction analyses (12).

Analysis of risk

Cases of recipient VAPP were classified as following the first dose of OPV or following subsequent feedings of OPV. The number of OPV doses distributed in Latin America between 1989 and 1991 (431 611 000 doses; PAHO unpublished data 1992) was used as the denominator to calculate the overall risk of recipient VAPP. We assumed that all infants would receive at least one dose of OPV by their first birthday; thus, the birth cohort for 1989–91 (39 663 000 live births, U.N. population data) was used as the denominator to calculate the risks of recipient VAPP related to the first-dose feeding of vaccine (5). The risks of recipient VAPP related to subsequent feedings of OPV were estimated by using as denominator the number of doses distributed in 1989–91 minus the birth cohort for that period. All risks were estimated by incorporating the 30% wastage that is thought to occur in Latin America when doses are distributed for use in the field. In so doing, risks are based on doses of OPV administered.

Traditionally, first- and subsequent-dose risks for contact VAPP each refer to the dose number of the recipient to whom the contact is exposed. This information was not available for contact VAPP cases, nor was information available to calculate risk by exposure to routine delivery versus mass campaign delivery of vaccine.

Analysis of cases with unknown neurological sequelae

A base case and two sensitivity analyses were conducted. The base case estimates of risk included VAPP cases (described above) with known neurological sequelae. To account for missing information among cases of AFP with unknown neurological sequelae, we carried out two sensitivity analyses.

For the first of these analyses, we added to the recipient VAPP cases from the base case analysis those AFP cases with a history of having received OPV 4–40 days prior to paralysis onset and who had unknown neurological sequelae as well as a diagnosis clinically compatible with poliomyelitis. Added to the contact VAPP cases from the base case analysis were AFP cases who had unknown neurological sequelae with a diagnosis clinically compatible with poliomyelitis and who had vaccine-related poliovirus isolated from their stools (excluding cases of recipient VAPP and culture-confirmed poliomyelitis).

For the second sensitivity analysis, we added to the total recipient VAPP cases from the first two analyses those AFP cases who had a history of having received OPV 4–40 days prior to paralysis onset as well as unknown neurological sequelae and an unknown clinical diagnosis. Added to the contact VAPP cases from the first sensitivity analysis were those AFP cases who had unknown neurological sequelae and unknown clinical diagnosis as well as vaccine-related poliovirus isolated from their stools.

The data were analysed using Lotus-123 and EPI INFO software provided by the Centers for Disease Control and Prevention, Atlanta, GA, USA. All statistical analyses were performed using χ^2 tests, with significance determined at the $P<0.05$ level.

Results

Of the 6043 cases of AFP reported in Latin America during 1989–91, 24% (1461/6043) exhibited neurological sequelae 60 days after paralysis onset, and 43% (2617/6043) had no sequelae. The latter cases were excluded from subsequent analyses. For the remaining 33% of the cases (1965/6043), it was not possible to determine the presence of neurological sequelae 60 days after paralysis onset.

Base case analysis

Risk of recipient VAPP with known neurological sequelae. Of the 1461 cases of AFP with neurological sequelae, data from 30 were excluded from further analyses because they were determined to be culture-confirmed cases of poliomyelitis due to wild poliovirus infections. Data for the remaining 1431 cases were then used to classify and evaluate the risk of VAPP.

Of the 1431 cases of AFP with neurological sequelae 60 days after paralysis onset, 102 (7%) cases of recipient VAPP were identified using a 4–30-day interval; 113 (8%), using a 4–35-day interval; 125 (9%), using the 4–40-day interval; and 138 (10%), using a 4–45-day interval. Regardless of the interval used, there were no significant differences in the distribution of age, gender, history of OPV vaccination, presence of fever at paralysis onset, or the final diagnosis reported. For all subsequent analyses of the risk of VAPP we therefore used a 4–40-day interval to define recipient VAPP, which allows for prodromal symptoms of up to 10 days and for more accurate comparisons with data from England and Wales and the USA.

Among the 125 recipient VAPP cases who had paralysis onset within 4–40 days of receiving OPV, 36 (29%) cases were diagnosed as GBS, 29 (23%) as clinically compatible poliomyelitis, three (2%) as tumour, one (1%) as trauma, 45 (36%) as other diagnoses (e.g., aseptic meningitis), and 11 (9%) as unknown. Compared with recipient VAPP cases diagnosed as GBS, recipient VAPP cases diagnosed as compatible with poliomyelitis were more likely to be <5 years of age ((93% (26/28); age of one case unknown) versus 67% (24/36), Yates' corrected $P = 0.03$) and to have fever at onset of paralysis (72% (21/29) versus 39% (14/36), Yates' corrected $P = 0.01$). These data suggest that cases occurring within 4–40 days of receipt of OPV, who are diagnosed as GBS, are unlikely to be true VAPP (11).

The overall risk in Latin America of recipient VAPP ($n = 125$) using a 4–40-day interval was estimated to be one case per 2.5 million doses administered and first-dose risk, one case per 1.0 million doses. When cases not likely to be paralytic poliomyelitis were removed from the analysis (36 cases with a diagnosis of GBS, 3 with tumour, and 1 case with trauma), the corrected overall risk using the remaining 85 recipient VAPP cases was one case per 3.6 million doses administered and the corrected first-dose risk was one case of VAPP per 1.2 million doses administered (Table 1).

Serotype-specific stool culture results for both uncorrected and corrected recipient VAPP are shown in Table 2. The effect of excluding those cases not

Table 1: **Risk of vaccine-associated paralytic poliomyelitis (VAPP), Latin America, 1989–91**

Type of case	Risk of:[a]		
	Recipient VAPP	Contact VAPP	Total VAPP
Known neurological sequelae:			
Overall risk	3.6 (85)[b]	5.6 (54)	2.2 (139)
First-dose risk	1.2 (24)		
Subsequent-dose risk	4.5 (61)		
Including unknown neurological sequelae and known final diagnosis:			
Overall risk	3.4 (89)	5.0 (61)	2.1 (150)
First-dose risk	1.1 (25)		
Subsequent-dose risk	4.3 (64)		
Including unknown neurological sequelae and unknown final diagnosis:			
Overall risk	2.7 (114)	3.3 (91)	1.5 (205)
First-dose risk	1.1 (27)		
Subsequent-dose risk	3.2 (87)		

[a] Shown is the ratio of one case to 10^6 doses. Corrected VAPP excludes cases with diagnoses unlikely to be true VAPP, i.e., trauma, tumour, transverse myelitis, and GBS.
[b] Figures in parentheses are the number of cases.

likely to be paralytic poliomyelitis (36 with a diagnosis of GBS, 3 with tumour, and 1 with trauma) resulted in a higher proportion of corrected recipient VAPP cases having vaccine-related poliovirus isolates compared with those not likely to be paralytic poliomyelitis. Of the 85 corrected recipient cases of VAPP, 31% (26/85) had vaccine-related poliovirus isolates compared with 5% (2/40) of the cases not likely to be paralytic poliomyelitis (Yates' corrected $P = 0.003$). Type 3 vaccine-related poliovirus were most frequently obtained from VAPP cases with one isolate. Thirteen of 26 recipient VAPP (corrected) cases (50%) with poliovirus isolates had a type 3 poliovirus isolated from their stools; the equivalent proportion for contact cases was 44%.

Risk of contact VAPP with known neurological sequelae. In the above analysis, 125 of the 1431 cases of AFP were analysed for recipient VAPP. The

remaining 1306 cases of AFP with neurological sequelae at 60 days after onset of paralysis (excluding recipient VAPP and culture-confirmed poliomyelitis) were included in the analysis of contact VAPP. Of these, 90 (7%) cases of contact VAPP with a vaccine-related poliovirus isolated from stools were identified: of these 90 cases, 73% (66/90) were less than 5 years of age; 32% (28/90) had less than three previous doses of OPV; and 59% (53/90) had fever at paralysis onset.

Of the 90 contact VAPP cases, 29 (32%) were diagnosed as GBS, 21 (23%) as poliomyelitis compatible, 4 (4%) as transverse myelitis, 2 (2%) as trauma, 1 (1%) as tumour, 23 (26%) as other diagnoses, and 10 (11%) as unknown. Compared with contact VAPP diagnosed as GBS, cases of contact VAPP that were diagnosed as poliomyelitis compatible were more likely to be under 5 years of age (90% (19/21) versus 55% (16/29); Yates' corrected

Table 2: **Isolates of vaccine-related polioviruses from cases of recipient and contact vaccine-associated paralytic poliomyelitis (VAPP), Latin America, 1989–91**[a]

	No. with an isolate	No. with:			No. with mixtures of isolates
		Type 1	Type 2	Type 3	
All recipient VAPP (n=125)	28	7	6	10	5[b]
Recipient VAPP (n=85, corrected)	26	6	5	10	5[b]
All contact VAPP (n=90)	90	32	19	23	16[c]
Contact VAPP (n=54, corrected)	54	15	13	19	7[d]

[a] Analysis limited to cases with known neurological sequelae.
[b] One mixture of type 2 and type 3 polioviruses; two mixtures of type 1 and type 2; and two mixtures of type 1, type 2, and type 3.
[c] Three mixtures of type 2 and type 3 polioviruses; eight mixtures of type 1, type 2, and type 3; two mixtures of type 1 and type 2; and three mixtures of type 1 and type 3.
[d] One mixture of type 2 and type 3 polioviruses; four mixtures of type 1, type 2, and type 3; one mixture of type 1 and type 2; and one mixture of type 1 and type 3.

$P = 0.02$). There was a non-significant trend for the latter group to more probably have had fever at onset of paralysis (76% (16/21) versus 52% (15/29); Yates' corrected $P = 0.16$). These data suggest that cases classified as contact VAPP who were diagnosed as GBS, transverse myelitis, trauma, and tumour were unlikely to be true paralytic poliomyelitis cases (9).

Among uncorrected cases of contact VAPP, vaccine-related type 1 polioviruses were the predominant isolates (Table 2). Compared with cases not likely to be VAPP, the distribution of vaccine-related poliovirus isolates among corrected cases of VAPP revealed a significantly greater proportion of type 3 and type 2 isolates ($P = 0.02$).

The estimated risk of uncorrected contact VAPP ($n = 90$) was one case of VAPP per 3.4 million doses of OPV administered. When the case definition was corrected by excluding cases not likely to be true paralytic poliomyelitis (29 with a diagnosis of GBS, 4 with transverse myelitis, 2 with trauma, and 1 with tumour), the corrected risk of contact VAPP ($n = 54$) was estimated to be one case per 5.6 million doses administered (Table 1). The total corrected risk of VAPP (for both recipient and contact VAPP, $n = 139$) was estimated to be one case per 2.2 million doses of OPV administered (Table 1).

Excluding those cases of recipient VAPP diagnosed to have GBS, transverse myelitis, trauma, or tumour, we plotted the 85 corrected recipient VAPP cases and 54 corrected contact VAPP cases according to date of onset of paralysis (Fig. 1) and by geographical location (Fig. 2). Most vaccination activities, including all national mass campaigns, occur between March and November in Latin America and

Fig. 1. **Cases of recipient and contact vaccine-associated paralytic poliomyelitis (VAPP), by month of onset, Latin America, 1989–91** (analysis limited to cases with known neurological sequelae).
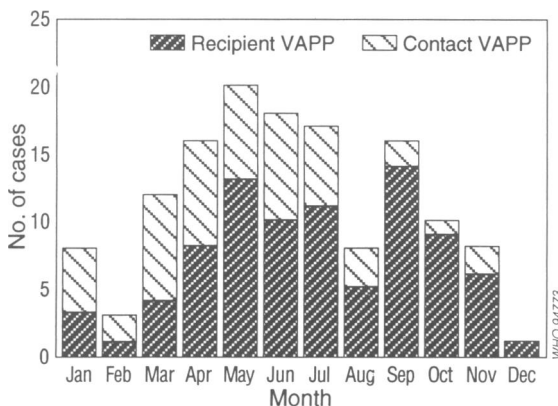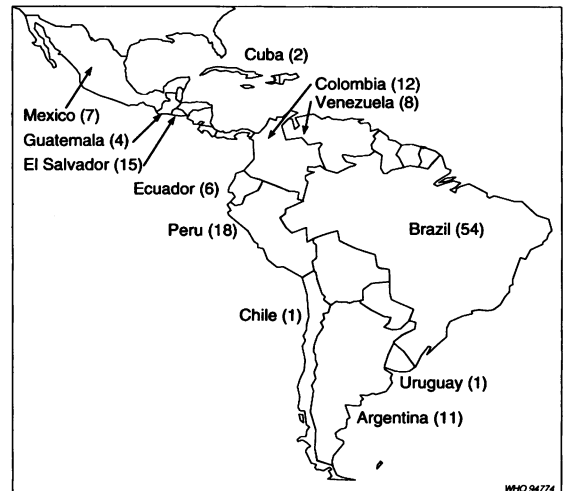

Fig. 2. **Cases ($n = 139$) of vaccine-associated paralytic poliomyelitis (VAPP), by country, Latin America, 1989–91** (analysis limited to cases with known neurological sequelae).

may explain the distribution of cases observed in Fig. 1. The highest number of VAPP cases ($n = 54$) was reported from Brazil.

First sensitivity analysis

Risk of recipient and contact VAPP, including cases with unknown neurological sequelae and known final diagnosis. Ten of the 1965 cases of AFP with unknown neurological sequelae were excluded from subsequent analyses because of the presence of wild poliovirus in their stools. Of the remaining 1955 cases, 5% (106/1955) had been fed OPV 4–40 days before the onset of paralysis. The distribution of clinical diagnoses among the 106 cases of AFP who met the OPV exposure criterion for recipient VAPP was as follows: 4% (4/106) for compatible poliomyelitis; 40% (42/106), GBS; 2% (2/106), trauma; 2% (2/106), transverse myelitis; 29% (31/106), other specific non-poliomyelitis diagnoses; and 23% (25/106), with unknown diagnosis.

In addition to the 85 cases of recipient VAPP with known sequelae were four AFP cases (1 first dose related and 3 subsequent doses) with unknown sequelae, who met the OPV exposure criteria and had a diagnosis of clinically compatible poliomyelitis.

Added to the 54 cases of contact VAPP with known sequelae in the base case analysis were 7 AFP cases with unknown sequelae, who had a diagnosis clinically compatible with poliomyelitis and vaccine-related poliovirus isolated from their stools.

First-dose risk of recipient VAPP ($n = 25$) was estimated to be one case per 1.1 million doses of OPV administered and the overall risk of VAPP ($n = 150$) was one case per 2.1 million doses administered.

Second sensitivity analysis

Risk of recipient and contact VAPP, including cases with unknown neurological sequelae and unknown clinical diagnosis.

In addition to the 89 cases of recipient VAPP identified above were 25 AFP cases (2 following the first dose of OPV and 23 following subsequent doses) who had unknown neurological sequelae and who met the OPV exposure criteria but who had unknown clinical diagnoses. Added to the 61 cases of contact VAPP were 30 AFP cases with unknown neurological sequelae and unknown clinical diagnoses and who had vaccine-related poliovirus isolated from their stools.

The first-dose risk of recipient VAPP ($n = 27$) was estimated to be one case per 1.1 million doses of OPV administered, while the overall risk of VAPP ($n = 205$) was one case per 1.5 million doses of OPV administered.

Discussion

In Latin America, the overall estimate of risk of VAPP was one case per 1.5–2.2 million doses of OPV administered, compared with one case per 1.4 million doses administered in England and Wales and one case per 2.5 million net doses distributed in the USA.

First-dose risk of recipient VAPP is more accurate for international comparisons because it is independent of vaccine wastage and the number of doses a child receives, which may be higher in countries that routinely use mass campaigns for eradication of poliomyelitis. First-dose risk also accounts for most of the risk of recipient VAPP. In Latin America first-dose risk of recipient VAPP was one case per 1.1–1.2 million doses of OPV administered, compared with one case per 0.7 million net doses distributed in the USA (5).

Subsequent-dose risk of recipient VAPP in Latin America appears to be substantially higher than in the USA. The following are possible explanations for this: the lower immunogenicity of OPV in developing countries; the higher rates of infection with other enteroviruses among children from developing countries; and/or problems with the cold chain that would compromise immunogenicity.

In this study, the nature of the residual paralysis 60 days after its onset could not be evaluated. Paralysis compatible with poliomyelitis begins with fever, and residual neurological deficit is usually proximal and asymmetrical; in contrast, GBS paralysis is more likely to be distal and involves all the extremities (13–15). However, the analysis validated the diagnosis previously made in the field. Compared with cases of VAPP diagnosed as GBS, cases of recipient VAPP that were compatible with poliomyelitis were younger and more likely to have fever at paralysis onset.

The data suggest that the isolation rates of vaccine-related poliovirus from cases not likely to be paralytic poliomyelitis were lower than cases whose diagnosis was consistent with true paralytic poliomyelitis. These findings, as well as the diagnostic experience of the field epidemiologists, appear to justify the exclusion of patients with GBS and other diagnoses easily distinguishable from poliomyelitis (trauma, tumour, or transverse myelitis) from subsequent risk analyses.

Throughout Latin America, more than 23 000 reporting health units comprise a comprehensive surveillance network to detect promptly all cases of AFP, whatever the cause. These units report weekly to central authorities whether or not cases of AFP have occurred (16). This surveillance is also supplemented with regular active case searches in areas such as the Amazon jungle of Brazil, Venezuela, Colombia, and Peru. Other case-finding activities include house-to-house searches when mass immunization campaigns are conducted and a financial reward system for people who report cases of poliomyelitis (3, 4). Together, these activities have identified a continuing incidence of approximately 2000 cases of AFP per year in Latin America. The proportion of cases associated with wild polioviruses has been declining steadily each year, with the last case reported in Peru in August 1991. Since 1987, the sensitivity of the surveillance system has been consistently maintained at >1.0 case of AFP reported per 100 000 population aged <15 years (the background rate for other causes of AFP such as GBS) (16).

Prior to 1978, when EPI was established in the Americas, a considerable proportion of the population in Latin America had naturally acquired immunity to poliomyelitis. Even though poliovirus vaccines were available before 1978, with the exception of that against smallpox, there had been no coordinated effort to administer vaccines, particularly to high-risk children. By 1985, when AFP surveillance criteria were being developed, essentially all cases of poliomyelitis that were reported involved under-15-year-olds.

Although the focus of surveillance is on children, criteria in Latin America require that AFP be reported if paralysis presents that is compatible with

poliomyelitis, regardless of age. We identified no adult cases of VAPP in the present study. From 1978 to 1991, the maximum age of children covered by EPI activities would have been 13 years. In view of the previous high endemicity and the relatively short era of immunization, the lack of sufficient numbers of adult susceptibles could explain the absence of adult VAPP in this investigation.

International comparisons of the risk of VAPP should be made with caution, since surveillance systems can differ between countries. By 1989, the AFP surveillance system in Latin America had been in operation for 3 years. Reporting of AFP cases is mandatory, and active and surveillance activities in Latin America are aggressively linked to immunization interventions, e.g., mass vaccination campaigns. Reporting of cases of poliomyelitis in the USA from 1980 to 1989 and in England and Wales from 1985 to 1991 was mandatory, but passive. In these countries only poliomyelitis cases were reported, hence the evaluation of all AFP cases was not possible.

Other considerations that account for variations in the risk of VAPP for subsequent doses of OPV include cold chain differences, vaccine failure, and the occurrence of outbreaks. Brazil, with 1.7 times the population of Mexico, was estimated to have nearly eight times the number of VAPP cases (54 for Brazil, 7 for Mexico); also, Brazil, which has approximately a third of the population of Latin America, accounted for 39% (54/139) of the VAPP cases in Latin America over the period 1989–91. Therefore, the reported number of cases of VAPP for Mexico may be less than the true incidence. One possible explanation for this is that an OPV with low type 3 potency was in use in Mexico in 1989–90 (4).

The poliomyelitis eradication surveillance system used by PAHO in Latin America is designed to monitor progress in eradicating transmission of indigenous wild poliovirus from the Americas. This focus inherently introduces difficulties in the assessment of the risk of VAPP. Despite this potential limitation, our analysis included the "universe" of AFP cases in Latin America, in which all cases of contact VAPP form an inclusive subset. We therefore carried out two sensitivity analyses to provide a range of estimates within which the true risk of VAPP probably lies.

The initiative to eradicate poliomyelitis in Latin America has relied heavily on the use of mass immunization campaigns to supplement delivery of OPV through routine immunization services (3, 4). It was recognized that in large underserved peri-urban populations use of multi-antigen national vaccination days was required to reach children who would otherwise have remained unimmunized. By "flooding" risk areas of the community with vaccine-related poliovirus, chains of transmission of wild poliovirus were abruptly interrupted (17). To define risk by type of dose (routine service administration versus campaign administration) and to define more accurately the risk of contact VAPP, we recommend that such information be collected routinely in the future.

Analysis of AFP surveillance data suggests that in Latin America there was no clear increase of risk of VAPP associated with the delivery of OPV through routine health services supplemented by mass immunization campaigns. In September 1990 the WHO Consultation Group on the Global Eradication of Poliomyelitis recommended that strategies similar to those used in the Americas be adopted by countries that are embarking on eradication of the disease. Our findings support this directive. As occurred with smallpox, we look forward to the date when the global eradication of poliomyelitis has been accomplished so that vaccination against it is no longer required.

Acknowledgements

Résumé

Risque de poliomyélite paralytique associée à la vaccination en Amérique latine, 1989–1991

La réussite des programmes d'éradication de la poliomyélite dans les Amériques repose en grande partie sur les campagnes de vaccination de masse par le vaccin antipoliomyélitique buccal (VPO). Avec l'accélération des activités d'éradication et l'adoption généralisée des campagnes de vaccination de masse, il est indispensable de déterminer si le risque de poliomyélite paralytique associée à la vaccination (PPAV) est modifié lorsque les stratégies habituelles d'administration du vaccin sont complétées par des campagnes de vaccination de masse. Afin d'évaluer ce risque, nous avons analysé les 6043 cas de paralysie flasque aiguë notifiés en Amérique latine en 1989–1991. Le risque global de PPAV en Amérique latine a été estimé à 1 cas pour 1,5–2,2 millions de doses de VPO administrées, contre 1 cas

pour 1,4 million de doses en Angleterre et au Pays de Galles (1985–1991) et 1 cas pour 2,5 millions de doses aux Etats-Unis d'Amérique (1980–1989). Ces données indiquent que pour éradiquer la poliomyélite à l'échelle mondiale, les stratégies fondées sur les campagnes de vaccination de masse en complément des services habituels d'administration des vaccins, telles qu'elles sont recommandées par l'OMS, ne semblent pas modifier de façon significative le risque de poliomyélite paralytique associée à la vaccination.

References

1. **Centers for Disease Control.** Update: eradication of paralytic poliomyelitis in the Americas. *Morbidity and mortality weekly report*, 1992, **41**(36): 681–683.
2. **Pan American Health Organization.** Director announces campaign to eradicate poliomyelitis from the Americas by 1990. *Bulletin of the Pan American Health Organization*, 1985, **19**: 213–215.
3. **de Quadros CA et al.** Eradication of poliomyelitis: progress in the Americas. *Pediatric infectious diseases journal*, 1991, **10**: 222–229.
4. **de Quadros CA et al.** Polio eradication from the Western Hemisphere. *Annual review of public health*, 1992, **13**: 239–252.
5. **Strebel PM et al.** Epidemiology of poliomyelitis in the United States one decade after the last reported case of indigenous wild-virus-associated disease. *Clinical infectious diseases*, 1992, **14**: 568–579.
6. **Joce R et al.** Paralytic poliomyelitis in England and Wales, 1985–1991. *British medical journal*, 1992, **305**: 79–82.
7. **Horstmann DM, Paul JR.** The incubation period in human poliomyelitis and its implications. *Journal of the American Medical Association*, 1947, **135**: 11–14.
8. **Casey A.E.** The incubation period in epidemic poliomyelitis. *Journal of the American Medical Association*, 1942, **120**: 805–807.
9. **Andrus JK et al.** Screening of cases of acute flaccid paralysis for poliomyelitis eradication: ways to improve specificity. *Bulletin of the World Health Organization*, 1992, **70**: 591–596.
10. **Melnick JL, Wenner HA, Phillips CA.** Enteroviruses. In: Lennette EH, Schmidt NJ, eds. *Diagnostic procedures of viral, rickettsial, and chlamydial infections*, 5th ed. Washington, DC, American Public Health Association, 1979: 471–534.
11. **Da Silva EE et al.** Oligonucleotide probes for the specific detection of wild poliovirus type 1 and type 3 endemic to Brazil. *Intervirology*, 1991, **32**: 149–159.
12. **Saika RK et al.** Primer-directed enzymatic amplification of DNA with thermostable DNA polymerase. *Science*, 1988, **239**: 487–491.
13. **Paul JR.** The clinical epidemiology of poliomyelitis. *Medicine*, 1941, **20**: 495–520.
14. **Asbury AK, Cornblath DR.** Assessment of current diagnostic criteria for Guillain-Barré syndrome. *Annals of neurology*, 1990, **27**(suppl.): S21–S24.
15. **Ropper AH.** The Guillain-Barré syndrome. *New England journal of medicine*, 1992, **326**: 1130–1136.
16. *Polio eradication field guide*. Washington, DC, Pan American Health Organization, 1994 (Technical Paper No. 40).
17. **Sabin AB et al.** Live, orally given poliovirus vaccine: effect of rapid mass immunization on population under conditions of massive enteric infections with other viruses. *Journal of the American Medical Association*, 1960, **173**: 1521–1526.